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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,922	08/29/2005	Gerard Papierok	1811-60	6168

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EGBERT LAW OFFICES
412 MAIN STREET, 7TH FLOOR
HOUSTON, TX 77002

EXAMINER

GANGLE, BRIAN J

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 09/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/521,922	Applicant(s) PAPIEROK ET AL.	
	Examiner Brian J. Gangle	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/29/2005</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-9 are currently pending and under examination.

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they do not include the following reference sign(s) mentioned in the description: Figures 1-5. These figures do not include reference signs because there are no figures in the application. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities: Trypan is improperly listed as a registered trademark.

Appropriate correction is required.

Information Disclosure Statement

The information disclosure statement filed 4/29/2005 has been considered. An initialed copy is enclosed. EPO 0301 961 has not been considered because no English translation is available. Said reference will be considered when a translation becomes available.

Claim Objections

Claim 2 is objected to because of the following informalities: the abbreviation Kda should be kDa. Appropriate correction is required.

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Claims 1-4 are objected to because of the following informalities: the term “characterized in that” is not preferred terminology in US patent applications. If the claimed molecules must have the recited limitations, it is not necessary to say that they are “characterized” by those limitations. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5-7 and 9 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 1-4 and 8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claimed invention is drawn to a product of nature. Products of nature are not patentable because they do not reflect the “hand of man” in the production of the product or manufacturing process. Immunoglobulins (including IgG2) are found naturally in animals.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

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art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to immunoglobulins characterized in that they are immunoglobulins of the classes IgG2 and corresponding sub-classes, specific to the excretion-secretion antigens of promastigotes or amastigotes of *Leishmania* sp., capable of lyzing the amastigotes and promastigotes of *Leishmania* sp. *in vitro* and neutralizing their proliferation (claim 1); wherein the immunoglobulins are specific to the major immunogen, excreted-secreted by promastigotes or amastigotes of *Leishmania* sp., belonging to the family of the Protein Surface Antigens and corresponding to a range of molecular mass from 52 to 58 kDa (claim 2); wherein the immunoglobulins are specific to the carboxyterminal part of the major excreted-secreted immunogen (claim 3); wherein the immunoglobulins are isotypes IgG2 in dogs and specific isotypes in other mammals, isotypes linked to cell-mediated immunity depending on T lymphocytes of the Th1 type (claim 4); wherein the immunoglobulins are effectors of immunotherapy in the context of leishmaniasis and infections by pathogenic intracellular microorganisms in mammals (claim 8).

The rejected claims are drawn to a genus of antibodies, the members of which bind to the "excretion-secretion antigens" of promastigotes or amastigotes of *Leishmania* sp. These antibodies must also have the capability to lyse said amastigotes and promastigotes and neutralize their proliferation. Dependent claims limit the genus to immunoglobulins that are specific to the major immunogen excreted-secreted by promastigotes or amastigotes of *Leishmania* sp., belonging to the family of the Protein Surface Antigens and corresponding to a range of molecular mass from 52 to 58 kDa, and to the carboxyterminal part of the major excreted-secreted immunogen.

The courts have recently decided in *Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin* (CAFC, 02-1187, 1/20/2004) that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or

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by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen. Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

In the instant application, Applicant has failed to "fully characterize" the antigen (i.e. excretion-secretion antigens) to which the claimed antibody binds. The instant claims are drawn to all immunoglobulins of the class IgG2 and corresponding subclasses with specificity to any antigen excreted or secreted by promastigotes or amastigotes of *Leishmania* sp., as long as said antibody is capable of lysing said promastigotes or amastigotes. Consequently, since Applicant has not fully characterized the antigen to which the claimed antibodies bind, the written description requirements under 35 U.S.C 112, first paragraph have not been met. To characterize an antigen, the immunoepitopes that can be found on said antigen must be identified. This characterization must not only include identification of epitopes that allow antigen:antibody binding, but also those that result in lysis of the microorganism.

The specification does not describe the excretion-secretion antigens to which the members of the claimed genus of antibodies must bind, such that the specification might reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at

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the time the application was filed. Further, the antigen to which the antibodies of claim 2 must bind is a Protein Surface Antigen, which, according to the art, is a membrane protein, and therefore cannot be excreted or secreted (see Kemp *et al.*, FEMS Immunol. Med. Microbiol., 20:209-218, 1998, IDS filed 4/29/2005).

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed.

See Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical

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formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

As evidenced by Greenspan et al. (Nature Biotechnology 17: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically. Even using a competition assay, the skilled artisan cannot determine whether an antibody binds the same epitope as another antibody because an antibody that competes with another does not necessarily bind the same epitope as the other; rather, one antibody may bind a spatially overlapping epitope to sterically hinder binding of the other. Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of epitopes to which the members of the claimed genus of antibodies must bind, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Moreover, since the specification has not identified which amino acids of the genus of epitopes to which the members of the claimed genus of antibodies must bind, which are critical or essential to the binding, one skilled in the art would not recognize that Applicant had possession of the claimed invention at the time the application was filed.

Therefore, in accordance with the *Guidelines*, the description of immunoglobulins is not deemed representative of the genus of immunoglobulins to which the claims refer.

Claims 1-4 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In *re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: The instant claims are drawn to immunoglobulins characterized in that they are immunoglobulins of the classes IgG2 and corresponding subclasses, specific to the excretion-secretion antigens of promastigotes or amastigotes of *Leishmania* sp., capable of lysing the amastigotes and promastigotes of *Leishmania* sp. *in vitro* and neutralizing their proliferation (claim 1); wherein the immunoglobulins are specific to the major immunogen, excreted-secreted by promastigotes or amastigotes of *Leishmania* sp., belonging to the family of the Protein Surface Antigens and corresponding to a range of molecular mass from 52 to 58 kDa (claim 2); wherein the immunoglobulins are specific to the carboxyterminal part of the major excreted-secreted immunogen (claim 3); wherein the immunoglobulins are isotypes IgG2 in dogs and specific isotypes in other mammals, isotypes linked to cell-mediated immunity depending on T lymphocytes of the Th1 type (claim 4); wherein the immunoglobulins are effectors of immunotherapy in the context of leishmaniases and infections by pathogenic intracellular micro-organisms in mammals (claim 8).

Breadth of the claims: The claims encompass the genus of immunoglobulins of the class IgG2 and corresponding subclasses, the members of which bind to the “excretion-secretion antigens” of promastigotes or amastigotes of *Leishmania* sp. These antibodies must also have the capability to lyse said amastigotes and promastigotes and neutralize their proliferation. Dependent claims limit the genus to immunoglobulins that are specific to the major immunogen excreted-secreted by promastigotes or amastigotes of *Leishmania* sp., belonging to the family of the Protein Surface Antigens and corresponding to a range of molecular mass from 52 to 58 kDa, and to the carboxyterminal part of the major excreted-secreted immunogen.

Working Examples/Guidance of Specification: The specification fails to describe either the antigens or the immunoepitopes against which the claimed antibodies are raised and must subsequently bind. Nor do they disclose which immunoepitopes would result in the lysis, and consequent neutralization of the promastigotes or amastigotes of *Leishmania* sp. “Excretion-secretion antigens” are not defined, and the “major immunogen” which belongs to the family of Protein Surface Antigens is described only in that it has a mass from 52 to 58 kDa. However, Protein Surface Antigens are membrane bound proteins, which, by definition, are not excreted or secreted. Further, there is no disclosure of antibodies that are specific to Protein Surface Antigens with a mass from 52 to 58 kDa, nor is there disclosure of any antibodies capable of lysing amastigotes or promastigotes of *Leishmania* sp., let alone antibodies specific to Protein Surface Antigens with a mass from 52 to 58 kDa that are capable of binding or lysing amastigotes or promastigotes of *Leishmania* sp.

State of the Prior Art and Unpredictability of the Art: In the instant application, Applicant has failed to “fully characterize” the antigen (i.e. excretion-secretion antigens) to which the claimed antibody binds. Consequently, since Applicant has not fully characterized the antigen to which the claimed antibodies bind, the skilled artisan would not be able to make the claimed invention.

While the skill in the art of immunology is high, to date, prediction of a specific immune response for any given composition in any given animal is quite unpredictable. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie *et al.* (Science, 1990, 247:1306-1310) teach that an amino acid sequence

encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie *et al.* further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie *et al.* further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Additionally, Greenspan *et al.* (Nature Biotechnology 17: 936-937, 1999), disclose defining epitopes is not as easy as it seems. Greenspan *et al.* recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan *et al.*, an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically. This constitutes undue experimentation. Therefore, given the lack of success in the art, the lack of working examples commensurate in scope to the claimed invention and the unpredictability of the generation of a directed immune response, the specification, as filed, is not enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered vague and indefinite by the phrase “the classes IgG2 and corresponding sub-classes.” There is no definition in the specification of the term “corresponding sub-classes.” What sub-classes correspond to IgG2? Further, the use of the phrase “classes IgG2” implies that there is more than one IgG2 class. What classes are meant to be included in the claims?

Claim 1 is rendered vague and indefinite by the phrase “excretion-secretion antigens.” There is no definition in the specification of an “excretion-secretion antigen.” It is not clear what the metes and bounds of the claimed invention are. Does “excretion-secretion antigen” include all compounds excreted or secreted by the organism, or does it include specific molecules such as proteins? And, if so, which proteins are included?

Claim 1 is rendered vague and indefinite because the claim is drawn to immunoglobulins capable of lysing amastigotes and promastigotes of *Leishmania*. Immunoglobulins are capable of inducing pathways which lead to lysis by other molecules, such as through the activation of the complement cascade, but are not capable of directly lysing cells.

Claim 2 is rendered vague and indefinite by the phrase “characterized in that they are specific to the major immunogen, excreted-secreted by promastigotes or amastigotes of *Leishmania* sp., belonging to the family of the Protein Surface Antigens and corresponding to a range of molecular mass from 52 to 58 kDa.” The use of commas and the sentence structure of this claim make it unclear which clauses apply to which subjects. Is applicant trying to state that the major immunogen is excreted-secreted by promastigotes or amastigotes, or that the immunoglobulins are excreted-secreted by promastigotes or amastigotes? Is the same molecule excreted-secreted by both promastigotes and amastigotes? It is unclear what is to have a molecular mass of 52 to 58 kDa. Is it the immunoglobulins, the major immunogen, or the Protein Surface Antigens that have this range? Further, how can a single immunogen have a range of weights? What is the major immunogen? What is meant by the term “excreted-secreted”? Is there a difference between antigens that are excreted and those that are secreted?

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In addition, the Protein Surface Antigens of *Leishmania* are membrane proteins; therefore, it is not clear how these proteins could be considered “excretion-secretion” antigens.

Claim 3 is rendered vague and indefinite by the phrase “specific to the carboxyterminal part of the major excreted-secreted immunogen.” What is the major immunogen? What is meant by the term “excreted-secreted”? Is there a difference between antigens that are excreted and those that are secreted? There is no definition provided in the specification for the term “carboxyterminal part.” It is unclear what limitations are engendered by this phrase. What are the limits of the “carboxyterminal part” of the immunogen?

Claims 4 and 8 are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. For example, what is meant by the term “effectors of immunotherapy” in claim 8?

Claims 5-7 and 9 provide for the use of the immunoglobulins of claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Deplazes *et al.* (Parasite Immunol., 17:451-458, 1995, IDS filed 4/29/2005).

The instant claims are drawn to immunoglobulins characterized in that they are immunoglobulins of the classes IgG2 and corresponding sub-classes, specific to the excretion-secretion antigens of promastigotes or amastigotes of *Leishmania* sp., capable of lysing the amastigotes and promastigotes of *Leishmania* sp. *in vitro* and neutralizing their proliferation

(claim 1); wherein the immunoglobulins are specific to the major immunogen, excreted-secreted by promastigotes or amastigotes of *Leishmania* sp., belonging to the family of the Protein Surface Antigens and corresponding to a range of molecular mass from 52 to 58 kDa (claim 2); wherein the immunoglobulins are specific to the carboxyterminal part of the major excreted-secreted immunogen (claim 3); wherein the immunoglobulins are isotypes IgG2 in dogs and specific isotypes in other mammals, isotypes linked to cell-mediated immunity depending on T lymphocytes of the Th1 type (claim 4); wherein the immunoglobulins are effectors of immunotherapy in the context of leishmaniasis and infections by pathogenic intracellular microorganisms in mammals (claim 8).

Deplazes *et al.* disclose IgG2 antibodies obtained from dogs that are infected with *Leishmania infantum* (see page 454, column 2, paragraph 2). Because the “excretion-secretion” antigens produced by promastigotes and amastigotes of *Leishmania* sp. are naturally produced by these organisms, a dog that is infected by *Leishmania infantum* would necessarily produce antibodies specific to the excretion-secretion antigens produced by promastigotes and amastigotes of *Leishmania* sp., including the major immunogen corresponding to a range of molecular mass from 52 to 58 kDa, and including antibodies specific to the carboxyterminal part of the major immunogen. Further, these antibodies would necessarily include antibodies having the same functional characteristics as the claimed antibodies. Finally, since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 1-4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Afrin *et al.* (Infect. Immun., 65:2371-2377, 1997).

The instant claims are drawn to immunoglobulins characterized in that they are immunoglobulins of the classes IgG2 and corresponding sub-classes, specific to the excretion-secretion antigens of promastigotes or amastigotes of *Leishmania* sp., capable of lysing the amastigotes and promastigotes of *Leishmania* sp. *in vitro* and neutralizing their proliferation (claim 1); wherein the immunoglobulins are specific to the major immunogen, excreted-secreted

by promastigotes or amastigotes of *Leishmania* sp., belonging to the family of the Protein Surface Antigens and corresponding to a range of molecular mass from 52 to 58 kDa (claim 2); wherein the immunoglobulins are specific to the carboxyterminal part of the major excreted-secreted immunogen (claim 3); wherein the immunoglobulins are isotypes IgG2 in dogs and specific isotypes in other mammals, isotypes linked to cell-mediated immunity depending on T lymphocytes of the Th1 type (claim 4); wherein the immunoglobulins are effectors of immunotherapy in the context of leishmaniasis and infections by pathogenic intracellular micro-organisms in mammals (claim 8).

Afrin *et al.* disclose IgG2 antibodies obtained from mice that have been immunized with *Leishmania donovani* promastigote antigens (see page 2372, column 1, paragraph 4). Because the Protein Surface Antigens produced by promastigotes and amastigotes of *Leishmania* sp. are naturally produced by these organisms, a mouse that is immunized with *Leishmania donovani* would have produced antibodies specific to the excretion-secretion antigens produced by promastigotes and amastigotes of *Leishmania* sp., including the major immunogen corresponding to a range of molecular mass from 52 to 58 kDa, and including antibodies specific to the carboxyterminal part of the major immunogen. Further, these antibodies would necessarily include antibodies having the same functional characteristics as the claimed antibodies. Finally, since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 1-4 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Sartori *et al.* (Clin. Exp. Immunol., 87:386-392, 1992).

The instant claims are drawn to immunoglobulins characterized in that they are immunoglobulins of the classes IgG2 and corresponding sub-classes, specific to the excretion-secretion antigens of promastigotes or amastigotes of *Leishmania* sp., capable of lysing the amastigotes and promastigotes of *Leishmania* sp. *in vitro* and neutralizing their proliferation (claim 1); wherein the immunoglobulins are specific to the major immunogen, excreted-secreted

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by promastigotes or amastigotes of *Leishmania* sp., belonging to the family of the Protein Surface Antigens and corresponding to a range of molecular mass from 52 to 58 kDa (claim 2); wherein the immunoglobulins are specific to the carboxyterminal part of the major excreted-secreted immunogen (claim 3); wherein the immunoglobulins are isotypes IgG2 in dogs and specific isotypes in other mammals, isotypes linked to cell-mediated immunity depending on T lymphocytes of the Th1 type (claim 4); wherein the immunoglobulins are effectors of immunotherapy in the context of leishmaniasis and infections by pathogenic intracellular microorganisms in mammals (claim 8).

Sartori *et al.* disclose IgG2 antibodies obtained from hamsters that have been infected with *Leishmania donovani* promastigote antigens (see page 389, column 1, paragraph 2). Because the Protein Surface Antigens produced by promastigotes and amastigotes of *Leishmania* sp. are naturally produced by these organisms, a hamster that is infected by *Leishmania donovani* would have produced antibodies specific to the excretion-secretion antigens produced by promastigotes and amastigotes of *Leishmania* sp., including the major immunogen corresponding to a range of molecular mass from 52 to 58 kDa, and including antibodies specific to the carboxyterminal part of the major immunogen. Sartori *et al.* show that the antigens to which the hamsters have been exposed include a 52 kD antigen from *Leishmania donovani*. Further, these antibodies would necessarily include antibodies having the same functional characteristics as the claimed antibodies. Finally, since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art reference, the burden is upon Applicant to show a distinction between the material, structural and functional characteristics of the claimed composition and the composition of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Conclusion

No claim is allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Mark Navarro can be reached on (571) 272-0861. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Brian Gangle
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ROBERT A. ZEMAN
PRIMARY EXAMINER